BIOC 482/552: Structural Biology

Credits: 3

Prerequisites: Concurrent or prior biochemistry; and freshman physics or equivalent

Date/Time/Place: Spring 2016, 10:00-10:50 AM, MWF, Keck Hall 107 MW and GEO 130 Fridays

Instructors: George N. Phillips (georgep@rice.edu), Ed Nikonowicz (edn@rice.edu)
TA: TBN Office hours by appointment.

Textbook/Readings: Lattman and Loll, Protein crystallography: A concise guide. 2008, Johns Hopkins Press (Kindle or Amazon), IUCr On-line dictionary of crystallography (free access),

Course Description: Structural biology plays an important role in defining atomic structures of biomolecules and understanding relationships between structure, dynamics and function. This course will give an introduction to techniques of determining bimolecular structures, X-ray crystallography, NMR, and cryoelectron microscopy and discuss striking examples of the power of structural biology including biomedical examples. It will provide knowledge of techniques used to obtain detailed structural and dynamic information about biological macromolecules. Designed for advanced undergraduates and beginning graduate students in the biological or physical sciences. Students will present short vignettes on interesting structural results and will design and print 3-D models on a color printer as a part of their presentation. There will be two short in-class exams, homework and a presentation with 3-D printer support, but no final exam. BIOC 553 students will be required to present two presentations. Mondays will be technology-related, Wednesdays will be structural biology examples in biomedicine, Fridays will be practical homework/discussion sections.

Course Objectives and expected learning outcomes:

- To introduce the fundamental theory and the practice of X-ray crystallography and NMR in modern structural biology and biomedicine
- To evaluate the research articles from the primary literature to understand and analyze advanced topics in X-ray crystallography, with an emphasis on fundamental principles, research methodologies, and emerging research topics.
- To improve scientific communication skills through explaining conclusions and methodology to the group and fielding questions.

Grading: Course grade based equally on three components. Homeworks, Exams, Presentation. Presentation will include production of a 3-D printed model of a macromolecule and a 20 minute talk.

Rice Honor Code: Students are required to use proper citations and follow other practices outlined in the Rice Honor Code information on Academic Fraud and Acknowledgement of Sources: http://honor.rice.edu/honor-system-handbook/

Accommodations for students with disabilities: Any student with a documented disability needing academic adjustments or accommodations is requested to speak with the instructor during the first two weeks of class. All discussions will remain confidential. Students with disabilities also should contact Disability Support Services in Allen Center.

Topics to be covered:
Overview of imaging and role of structural methods in modern science

Symmetry (point groups, 2D, 3D, icosahedra: Crystallization of proteins

Diffraction from cyrstalline objects, Reciprocal space

Electron density equation, Phase problem, Patterson function, Heavy atom/direct methods, isomorphous replacement

Molecular replacement, Non-crystallographic averaging, refinement, Laue methods, synchrotrons, phasing

X-ray fiber diffraction, solution scattering

NMR methods of structure determination

High resolution electron microscopy

Molecular Dynamics Simulations

Analysis of electrostatics of proteins

Structure-based drug design

Student and others' presentations on interesting biological systems and 3-d printing of molecules

Preliminary Schedule

Week 1

	Introduction to class and requirements
Jan 11	Brief overview of crystallography and NMR and their roles in science Review of macromolecules and their general structure Review of complex numbers and operators needed in the class Scattering and illustration of how diffraction is the sum of waves Comparison of imaging methods in biology
Jan 13	Introduction to enzymes that make natural products, Jerry Wang
Jan 15	Pymol Tutorial Session (Weiss Computer lab)

Week 2

Jan 18	No class – MLK Day
Jan 20	Lattices, unit cells Symmetry Space groups Crystallization theory Miller indices
Jan 22	Crystallization demonstration

Week 3

Jan 25	Diffraction from lattices Reciprocal Space Bragg's Law X-ray sources Crystal mounting Data collection and reduction
Jan 27	Enzymes that make Antibiotics - Jerry Wang
Jan 29	X-RayView exercises 1-d transform exercise Laser/EMgrid demonstration

Week 4

Feb 1	Electron density equation The Phase Problem Fourier transform pairs and convolution theorum Solving the phase problem Heavy atoms Patterson Function/Anomalous scattering
Feb 3	Space Group determination in practice, data processing methods
Feb 5	More X-RayView exercises

Week 5

Feb 8	Phase problem continued, molecular replacement Intro to electron density maps, phase Bias Difference maps Refinement and Cross-validation Fitting electron density maps Difference Maps Specialized Maps
Feb 10	Motions in crystals and Displacement parameters – B-factors
Feb 12	Electron Density fitting

Week 6

Feb 15	Diffraction from helices Discovery of the double helix Validation of results/PDB Overview of crystallography - Review
Feb 17	GPCR's and Membrane Signaling - Phillips
Feb 19	Crystallography EXAM/Homework completion

Week 7

Feb 22	Molecular Dynamics Theory Electrostatics theory Alchemical transformations The folding of a protein *in silico* - Phillips
Feb 24	Docking and structure-based drug design - Phillips
Feb 26`	NAMD exercise

Spring Break

Week 8

Mar 7	Electron microscopy Single particle Practical EM Solution Scattering and examples Diffraction from membranes and examples
Mar 9	The structural biology and pathology of muscle contraction -Phillips
Mar 11	Exercise on solution scattering, more Pymol

Week 9

Mar 14	Protein folding – Anfinsen dogma Measurement of folding/unfolding Homology Modeling BLAST
Mar 16	The folding of a protein *in silico* - Phillips
Mar 18	BLAST/homology exercise, finish model to be printed

Week 10

Mar 21	Basics of NMR One- and Two-dimensional NMR
Mar 23	Structural constraints from NMR The phenomenon of chemical exchange
Mar 25	Time scales of molecular and atomic motions Structural characterization of sparsely populated states

Week 11

Mar 28	Relaxation-dispersion and measuring microsecond timescale motions
Mar 30	Additional types of structure constraints Residual dipolar couplings

	Chemical shift tensors
Apr 1	**Mid-Term Recess**

Week 12

Apr 4	Dealing with the molecular size problem
	Transverse Relaxation Optimized Spectroscopy
	Random fractional deuteration
Apr 6	Application to *really* big complexes
Apr 8	NMR/MD/EM EXAM

Week 13

Apr 11	Student presentations
Apr 13	Student presentations
Apr 15	Student presentations

Week 14

Apr 18	Student presentations
Apr 20	Student presentations
Apr 22	Student presentations